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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/555,473 | 05/31/2000 | BARBARA BOTTAZZI | 2801-18 | 9420 |

23117 7590 10/05/2006

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| EXAMINER | |
|---|---|
| ROONEY, NORA MAUREEN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

DATE MAILED: 10/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/555,473 | BOTTAZZI ET AL. | |
| | Examiner | Art Unit | |
| | Nora M. Rooney | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any paper for this application, all further correspondence regarding this application should be directed to Nora M. Rooney, Art Unit 1644, Technology Center 1600.

2. Applicant's amendment filed 07/10/2006 is acknowledged.

3. Claims 17-19 are pending

4. The specification on page 12 is objected to because of the following informalities:
"FTX3" on line 11 should be changed to --PTX3--; and
"FITX3" on line 18 should be changed to --PTX3--.

### *Claim Rejections - 35 USC § 102*

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Alles et al. *Blood*, 84(10):3483-3493 (1994), of record.

Alles et al. teaches 1.) a composition comprising naturally occurring human PTX3 from human peripheral blood mononuclear cells and a pharmacologically acceptable excipient (i.e. saline) injected subcutaneously into an animal (entire document, in particular, pages 3483-3485 and 3489); and 2.) mature human PTX3 protein isolated

from the supernatant of COS cells incubated in DMEM for Western analyses (in particular pages 3485.

A composition is a composition, regardless of its intended use. Therefore, the reference teachings anticipate the claimed invention.

Previous applicant arguments have been fully considered, but have not been found convincing.

A. Claim 17 is anticipated by PTX3 isolated from a gel, disrupted in saline and injected into an animal.

Applicant argues in the response filed on 11/20/2002 that "a pharmaceutical composition is a mixture composed of an active ingredient and at least a pharmaceutically acceptable excipient. "'Pharmaceutical acceptable excipient(s)' are an excipient or a mixture of excipients which do not give rise to unwanted toxic side effects." Because the composition mentioned in Alles et al. is composed of PTX3, polyacrylamide and saline, applicant argues, the admixture has toxic effects and cannot be a pharmaceutical composition.

In the Alles et al. reference, PTX3 protein is administered in saline, a known and accepted excipient, to an animal. Therefore, it is being used in the reference as a pharmaceutical, regardless of any toxicity the animal may or may not experience from conditions resulting from being isolated from polyacrylamide. Many pharmaceutical compositions elicit toxic side effects, nonetheless, they are still pharmaceuticals. Since applicant's claims are not directed specifically to human subjects, the FDA regulations regarding pharmaceutical preparations and the guidelines thereto are not persuasive. But, even if the claims were limited to human use, the reference teachings anticipate the claimed invention because the specification provides no guidance regarding toxicity level of the pharmaceutical composition.

The reference teachings anticipate the claimed invention. The prior art teaches the same product. Intended uses do not carry patentable weight *per se*, as the claims read on the active or essential ingredients of the PTX3.

B. Claim 17 is anticipated by PTX3 protein in COS cell supernatant containing DMEM.

Applicant argues in the response filed 1/16/2004 by argument and by declaration that DMEM is not a pharmaceutically acceptable excipient. The supernatant of Alles et al. is not expected to be an administrable pharmaceutical composition because it is "more likely than not that the solutions of Alles contain, for example, COS cells metabolites, catabolite and residual components of the cellular lysis, such as virus related or released by the DNA of the COS cells."

Since the specification does not provide any limiting definition of pharmaceutical carriers, the prior art's DMEM would appear to be encompassed by the broadest reasonable definition of a "pharmaceutically acceptable excipient." Giving the term its broadest reasonable definition, DMEM is not incompatible with pharmaceutical use; therefore it is encompassed by the term.

PTX3 in DMEM solution, which may contain "metabolites, catabolite and residual components of the cellular lysis, such as virus related or released by the DNA of the COS cells", is still a pharmaceutical composition. The term "containing" in Claim 17 is open language allowing for the pharmaceutical composition to contain substances other than PTX3 and a pharmaceutically acceptable excipient, such as the aforesaid metabolites. FDA regulations regarding pharmaceutical preparations and the guidelines thereto are not persuasive in the instant case, as the claims are not limited to human use. However, even if the claims were limited to human use, the reference teachings anticipate the claimed invention because the specification provides no guidance as to the level of purity of the pharmaceutical composition. Therefore, PTX3 in DMEM solution containing potential impurities is "not incompatible with pharmaceutical use."

The reference teachings anticipate the claimed invention.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 17-19 are rejected under 35 U.S.C. 103(a) as being anticipated by Gewurz et al., Current Opinion in Immunology 7:54-64 (1995) (PTO-892), in view of U.S. Patent No. 5,426,181, of record.

Gewurz teaches 1.) the TSG-14/PTX3 molecule is homologous to the pentraxin family of proteins comprising c-reactive protein (CRP) and shows immunological cross-reactivity with human CRP (in particular, pages 54 and 57); 2.) CRP activates the classic complement pathway and binds C1q (in particular, page 58); 3.) the pentraxin family of molecules bind neutrophils, macrophages and natural killer cells (in particular, page 59) and 4.) CRP elicits anti-tumor activity (in particular, pages 59-60).

PTX3/TSG-14 is a pentraxin family member homologous to CRP. CRP is known to bind C1q and leukocytes and to promote inflammation and elicit anti-tumor activity.

The claimed invention differs from the Gewurz et al. reference teachings only by the recitation of a pharmaceutical excipient in claim 17.

The 5,426,181 reference teaches TSG-14, known in the prior art as the same molecule as PTX3 (see Gewurz et al., in particular page 56), having a human sequence of 381 amino acids that is identical, with the exception of one amino acid, to SEQ ID NO. 1 of the instant application. The reference teaches the TSG-14 protein in a pharmaceutical composition with a pharmaceutically acceptable excipient for the treatment of tumors or infections (in particular, column 6, lines 56-57 and columns 32-34).

Given the homology of PTX3 to CRP, another pentraxin family member shown to activate complement, bind leukocytes and elicit anti-tumor activity, one of ordinary skill in the art at the time the invention was made would have been motivated to use the PTX3 protein as a pharmaceutical composition. One of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention because the'181 reference taught a pharmaceutical composition with a protein known in the art to be the same protein as that claimed and a pharmaceutical excipient for treatment of cancer and infections.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina

Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 28, 2006

Nora M. Rooney, M.S., J.D.
Patent Examiner
Technology Center 1600

Maher M Haddad

MAHER M. HADDAD
PATENT EXAMINER